

**AMENDMENTS TO THE SPECIFICATION:**

Please replace the paragraph at p. 22, lines 16-24 with the following amended paragraph:

This invention concerns chromosome specific reagents and methods of staining targeted chromosomal material that is in the vicinity of a suspected genetic earrangement rearrangement. Such genetic rearrangement rearrangements include but are not limited to translocations, inversions, insertions, amplifications and deletions. Aneuploidy is included herein in the term "amplifications". When such a genetic rearrangement is associated with a disease, such chromosome specific reagents are referred to as disease specific reagents or probes. When such a genetic rearrangement is associated with cancer, such reagents are referred to as tumor specific reagents or probes.

Please replace the paragraph at p. 36, lines 5-9 with the following amended paragraph:

c. Section (c) represents the use of a probe which binds to sequences which come together as a result of the rearrangement and allows for the detection in metaphase and interphase cells. In this case the different sequences are stained with different "colors". Such a staining pattern is that used in the examples of Section VIII of the this application.

Please replace the paragraph at p. 37, line 9 to p. 38, line 5 with the following amended paragraph:

Figure 13 shows FISH with fourteen Rb-1 lambda phage clones (Rb-1 probe) in normal and abnormal metaphase spreads and interphase nuclei. Panels A and B show two pairs of bright and specific hybridization signals on normal lymphocyte metaphase preparations in the mid-region of the q-arm of chromosome 13. Panel B further shows cohybridization with a 13/21 centromeric probe. Panel C shows a digital image analysis of the mapping of the Rb-1 gene on a metaphase chromosome using both the Rb-1 probe and the 13/21 centromeric-specific repeat probe. Panel D shows two bright and specific

hybridization domains in interphase nuclei of normal lymphocytes. Panel E shows cohybridization of the Rb-1 probe and a 13/21 centromeric-specific repeat probe to metaphase spreads of a fibroblast cell line (GM05877) derived from a sporadic retinoblastoma patient. Intact chromosome 13s show both Rb-1 and centromere signals; whereas chromosome 13s with a Rb-1 deletion are slightly shortened and hybridize only with the centromeric probe. Panel F shows a digital image analysis of the GM05887 cell line metaphase showing both the normal and shortened chromosome 13 and wherein cohybridization was effected with both the Rb-1 and 1/321 centromeric probe. Panel G shows hybridization of the Rb-1 probe to a GM05887 cell line interphase. Panel H shows hybridization of the Rb-1 probe to a clinical breast cancer specimen. Panel I shows a digital image analysis of a dual color hybridization to a normal interphase nucleus; differently labeled ~~portions~~ portions of the Rb-1 probe – a 3' (green) portion and a 5' (red) portion – were hybridized to the normal interphase nucleus.

Please replace the paragraph at p. 39, lines 3-18 with the following amended paragraph:

Figure 17 shows simultaneous hybridization with a chromosome 3 centromeric-specific probe generated by the polymerase chain reaction (PCR) and a chromosome 3 locus-specific cosmid probe (mapped to ch. 3q26 by digital image analysis). Panel A shows such a hybridization to metaphase spreads and interphase nuclei from normal lymphocytes wherein two chromosome 3 centromeric-specific signals (indicated by short arrows) and two pairs of chromosome 3q cosmid signals (indicated by long arrows) are clearly visible in the metaphase spreads; and wherein two large hybridization domains for the chromosome 3 centromere and two small domains for the chromosome 3q locus-specific probe are visible in the interphase nuclei. Panel B shows such a ~~hybridization~~ hybridization to a uterine cervical adenocarcinoma cell line (TMCC-1) wherein two chromosome 3 centromere-specific (indicated by short arrows) and two chromosome 3q locus-specific cosmid (indicated by

large arrows) signals are clearly visible in metaphase spreads whereas a pair of cosmid signals specific to chromosome 3q are found to be translocated to another chromosome.

Please replace the paragraph at p. 73, line 19 – p. 74, line 5 with the following amended paragraph:

3.c.i. Hydroxyapatite. Single- and double-stranded nucleic acids have different binding characteristics to hydroxyapatite. Such characteristics provide a basis commonly used for fractionating nucleic acids. Hydroxyapatite is ~~commercially~~ commercially available (eg. Bio-Rad Laboratories, Richmond, CA). The fraction of genomic DNA containing sequences with a particular degree of repetition, from the highest copy-number to single-copy, can be obtained by denaturing genomic DNA, allowing it to reassociate under appropriate conditions to a particular value of  $C_o t$ , followed by separation using hydroxyapatite. The single- and double-stranded nucleic acid can also be discriminated by the use of S1 nuclease. Such techniques and the concept of  $C_o t$  are explained in Britten et al., "Analysis of Repeating DNA sequences by Reassociation, in Methods in Enzymology, Vol. 29, pgs. 363-418 (1974), which article is herein incorporated by reference.